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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/608,713	06/30/2000	Hideo Ago	SHIM-007	2056

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EXAMINER

LY, CHEYNE D

ART UNIT PAPER NUMBER

1631

DATE MAILED: 10/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Advisory Action</b>	Application No. 09/608,713	Applicant(s) AGO ET AL.	
	Examiner Cheyne D Ly	Art Unit 1631	

**--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

THE REPLY FILED 14 September 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

**PERIOD FOR REPLY [check either a) or b)]**

- a) ☐ The period for reply expires \_\_\_\_\_ months from the mailing date of the final rejection.
- b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☒ A Notice of Appeal was filed on 14 September 2004. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☒ The proposed amendment(s) will not be entered because:
- (a) ☒ they raise new issues that would require further consideration and/or search (see NOTE below);
  - (b) ☐ they raise the issue of new matter (see Note below);
  - (c) ☒ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
  - (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: See Continuation Sheet.

3. ☐ Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.
4. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☒ For purposes of Appeal, the proposed amendment(s) a) ☒ will not be entered or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: \_\_\_\_\_.

Claim(s) objected to: \_\_\_\_\_.

Claim(s) rejected: 30,31,33,38 and 39.

Claim(s) withdrawn from consideration: \_\_\_\_\_.

8. ☐ The drawing correction filed on \_\_\_\_\_ is a) ☐ approved or b) ☐ disapproved by the Examiner.
9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_\_.
10. ☒ Other: See Continuation Sheet

Continuation of 2. NOTE: The new limitation of "and wherein...an NS5B HCV polymerase" in lines 18-20 of claim 30 raises new issues that would require further consideration and/or search. Therefore, the proposed claims amendments filed September 14, 2004 have not been entered.

Continuation of 5. does NOT place the application in condition for allowance because: Applicant's argument and amendments are not deemed to be persuasive to overcome the 35 U.S.C. §112, first paragraph, New Matter rejection and lack of enablement in scope rejection, and the 35 U.S.C. § 103(a) prior art rejection as discussed below.

Claims 30, 31, and 38 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

This NEW MATTER rejection is maintained with respect to claims 30, 31, and 38 as recited in the previous Office Action, mailed June 14, 2004. Applicant's argument via the proposed claim amendments is not persuasive because of the non-entry of the proposed claims amendments.

Claims 30, 31, 33, 38, and 39 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a crystal structure of HCV polymerase using NS5B570, 544, 536 and 531, does not reasonably provide enablement for all HCV polymerases. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

This rejection is maintained with respect to claims 30, 31, 33, 38, and 39 as recited in the previous Office Action, mailed June 14, 2004.

Applicant argues that the specification fully enables the claims as amended. It is noted that the claims amendments have not been entered as discussed above. Further, Applicant's argument has been fully considered and found to be unpersuasive because the newly added limitations above do not limit the claimed invention to what is enabled by the instant specification.

Claims 30, 31, 33, 38, and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kim et al. (US 6,183,121 B1) in view of In re Gulack, 703 F.2d 1381, 1385, 217 USPQ 401, 404 (Fed. Cir. 1983) taken with Bressanelli et al. (1999).

This rejection is maintained with respect to claims 30, 31, 33, 38 and 39 as recited in the previous Office Action, mailed June 14, 2004.

Specific to Applicant's argument directed to In re Gulack, the legal decision as discussed in In re Gulack has been applied to the instant rejection to support the non-functional descriptive material does not distinguish the invention from the prior art in term of patentability. Further, Applicant argues that the instant invention is directed to methods of interpreting complex three-dimensional molecular structure with structural resolutions on the order of Angstroms, not printed lines and characters. Applicant is directed Table 2 (beginning on page 26) of the instant wherein the complex three-dimensional molecular structure with structural resolutions on the order of Angstroms are printed lines and characters to be interpreted by the claimed method.

Specific to Applicant's argument directed to Kim et al., Kim et al. discloses the method steps for identifying an inhibitor from using the three-dimensional coordinates of a polypeptide as required by the instant claims. As noted in the previous Office Action, Kim et al. does not specify that the three-dimensional structural coordinates be derived from a NS5B HCV polymerase as required by the instant method claims. However, the specific limitation of three-dimensional structural coordinate being derived from a HCV polymerase in this instant case does not distinguish the invention from the prior art in term of patentability because they are descriptive nonfunctional subject matter.

Specific to Applicant's argument of no motivation to combine the references of Bressanelli et al. and Kim et al., Kim et al. discloses that "[a]n understanding of such associations will help lead to the design of drugs having more favorable associations with their target receptor or enzyme, and thus, improved biological effects. Therefore, this information is valuable in designing potential inhibitors of the binding sites of biologically important targets" (column 6, lines 23-29). The polypeptide, NS3 helicase, of Kim et al. is a derivative of NS5B HCV polymerase (column 1, lines 47-67). Therefore, one of ordinary skill in the art at the time of the instant invention would have been motivated by the improvement disclosed by Kim et al. for a method that uses molecular design techniques to identify, select and design chemical entities, including inhibitory compounds based on the 3-dimensional structure of a polymerase (Column 14, lines 27-38) and apply such method to the crystal structure for RNA-dependent RNA polymerase of hepatitis C virus as disclosed by Bressanelli et al.

Specific to Applicant's argument of "no reasonable expectation of success", said argument is directed to the difference in the way data used in the respective methods of Kim et al. and Bressanelli et al. have been obtained. Kim et al. discloses that "a computer which, when programmed with at least a portion of the structural coordinates of HCV NS3 helicase and an X-ray diffraction data set of a different molecule or molecular complex, performs a Fourier transform of these structural coordinates of the helicase coordinates and then processes the X-ray diffraction data into structure coordinates of the different molecule or molecular complex via the process of molecular replacement." Further, Kim et al. discloses the polypeptide, NS3 helicase, is a derivative of NS5B HCV polymerase (column 1, lines 47-67). The disclosure cited above suggests that one of ordinary skill in the art at the time of the instant invention would have reasonable expectation of success from combining the disclosure of Kim et al. and Bressanelli et al. in a method for identifying inhibitors of based on HCV helicase or HCV polymerase structure data.

Continuation of 10. Other: Applicant argues that the Office has mischaracterized Applicant's benefit of priority to applications JAPAN 11-188630, filed July 02, 1999, and JAPAN 11-192488, filed July 07, 1999. Applicant's argument has been fully considered and found to be unpersuasive. The foreign priority benefit has not been granted because the foreign applications are directed to a generic HCV

polymerase while the instant claimed invention is directed to a limited NS5B HCV polymerase. Therefore, the instant application does not receive the priority benefit of foreign applications JAPAN 11-188630, filed July 02, 1999, and JAPAN 11-192488, filed July 07, 1999, as directed to the limitation of NS5B HCV polymerase. However, the benefit of priority for the subject matter in common between the instant application and the two priority applications JP 11-188630, filed July 2, 1999, and JP 11-192488, filed July 7, 1999, has been granted.

It is noted that the disclosure of Kim et al. (US 6,183,121 B1), as directed to the subject matter in common between the instant application and the two priority applications, has a 102(e) date of August 03, 1998 which is prior to the earliest priority date. Further, the disclosure of Bressanelli et al., as directed to the limitation of NS5B HCV polymerase which does not receive any priority benefits, has a publication date of 1999 which is prior to the instant Application filing date.

*Ardin H. Marschel* 10/13/04  
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PRIMARY EXAMINER